1. DESCRIPTION OF MEDICINAL PRODUCT

1.1 NAME: Stabilanol


2. PHARMACEUTICAL FORM:
Capsules. Solution for intravenous infusion.

3. STRENGTH OF ACTIVE SUBSTANCE:
• Capsules: 50mg, 100mg, 150mg.

4. Solution for intravenous infusion: 50mg, 100mg/50ml (Vial) 100mg/50ml (Vial).

5. DESCRIPTION - PACKAGE:
• Capsules 50mg: Cardboard pack containing 7 capsules in transparent PVC/Aluminium blister with patient information leaflet.

• Capsules 100mg: a) Cardboard pack containing 7 capsules in transparent PVC/Aluminium blister with instructions on usage b) Cardboard pack containing 14 capsules placed in 2 transparent PVC/Aluminium blisters with patient information leaflet.

• Capsules 150mg: Cardboard pack containing 1 capsule in transparent PVC/Aluminium blister with information leaflet.

• Solution for intravenous infusion: Cardboard pack containing a transparent glass vial of 50ml sealed with a rubber stopper and aluminium cap; with patient information leaflet.

6. THERAPEUTIC CATEGORY:
Antifungal agent.

7. MARKETING AUTHORITY HOLDER / MANUFACTURER:
PHARMATHEN S.A., 6, DERVENAKION STR., 153 51 PALLINI ATTIKIS, MARKETING AUTHORIZATION HOLDER / MANUFACTURER.

8. INFORMATION REGARDING THE MEDICINE PRESCRIBED FOR YOU BY YOUR DOCTOR

2.1 GENERAL INFORMATION:
FLUCONAZOLE belongs to a group of medicines called the triazole antifungal agents and is a potent and specific inhibitor of sterol synthesis in fungi.

2.2 INDICATIONS:
Systemic mycoses:
1. Cryptococcal infections including cryptococcal meningitis and infections of other areas (e.g. lungs, skin, AIDS patients, as well as patients who have undergone an organ transplant or present other causes of immunosuppression may be treated. Fluconazole may be used for the prevention of recurrent cryptococcal diseases in AIDS patients.

2. Generalized candidiasis including candidemia in clinically stable and non-neutropenic patients, diffuse and metastatic candidiasis (infections of the peripheral blood and central nervous system, as well as lung and urinary tract infections). Patients with malignant neoplasms or in intensive care units, as well as patients receiving cytostatic or immunosuppressive drugs or patients presenting other factors in favor of candidiasis may also be treated with the drug. It is self-evident that for indications 1 and 2, cultures and proper laboratory examinations should be conducted before the initiation of the treatment (immediate microscopic examination, biopsies, serum examinations), in order to isolate and identify the causative factor.

3. Deep endemic mycoses, such as coccidioidomycosis, paracoccidioidomycosis, sporotrichosis and histoplasmosis in immunocompetent patients.

4. Mycosal candidiasis. This includes oropharyngeal and esophageal candidiasis (as an alternative to topical treatment), non-invasive bronchopulmonary candidiasis. Candiduria, chronic mucocutanous candidiasis. Chronic atrophic oral candidiasis (stomatitis due to dentures), as an alternative to local treatment. Patients mostly with immune system disorders can undergo a treatment with the drug.

5. Gential candidiasis:
Vaginal candidiasis as an alternative to topical treatment (only as single dose of 150mg)

a) acute
b) relapsing as long as the infection has been confirmed by culture (usually of non-inflammatory cause but due to allergy or hypersensitivity).

Candidal balanitis.

6. Dermatophytois including infections of the foot, of the thin skin layer and of the skin of the head line, as well as tinea versicolor; onychomycosis and infections caused by CANDIDA.

Note: Systemic treatment in the case of the indications mentioned above is preferable when the infection extends to a large skin area or the scalp, or in patients with disorders of defense mechanisms, unresponsive to local treatment and persistence of the mycotic infection despite treatment.

7. Prevention of candidiasis in patients with neutropenia and malignant diseases that predispose to the development of such infections as a result of chemotherapy and/or radiotherapy in cases of marrow transplantation. Caution: chronic administration of azoles increases the possibility of development of C. KRUSEI, ASPERGILLUS, MUCORALES, PUSARIUM, T. GLABRATA that usually present a natural resistance to azoles. Therapy may be initiated before the results of the cultures and other laboratory studies are known. However when the results are known, therapy should be adjusted accordingly.

2.3 Contra-indications:
Stabilanol should not be administered in patients with known sensitivity to Fluconazole or to the excipients or to related azole preparations.
Co-administration of chlorthiazide is contra-indicated in patients receiving fluconazole.
Based on the results of a multiple dose interaction study, co-administration of terfenadine in patients receiving fluconazole at doses of 400 mg or more per day is contraindicated.

2.4 Special warnings and special precautions for use:

2.4.1 General:
Hepatic failure: the administration of fluconazole has been correlated in rare cases to severe hepatotoxicity which in exceptional cases has led to failure, especially in patients with severe illness in patients taking fluconazole and in the absence of total daily dose, the duration of the therapy, gender or age was observed. Hepatotoxicity from fluconazole is usually, but not always, reversible, after treatment withdrawal.

Patients with biochemical disturbances of hepatic function throughout the duration of treatment with fluconazole, must be closely monitored for the possibility of developing severe hepatotoxic failure. Fluconazole should be discontinued if clinical signs and symptoms of hepatic disease are observed. Rarely, patients have developed exfoliative dermal cutaneous reactions such as Steven-Johnson syndrome or a bullous epidermal necrolysis erythema during treatment with fluconazole. Patients with AIDS are more prone to the development of severe cutaneous reactions with many drugs. If a rash develops in patients treated for superficial fungal infections which is considered attributable to fluconazole, therapy should be discontinued. If patients with invasive/systemic fungal infections develop rashes, they should be monitored closely and treatment with Fluconazole should be discontinued if bullous lesions or erythema multiforme develop.

In rare cases, anaphylaxis has been reported.

2.4.2 Administration in the elderly:
If there are no indication of renal function impairment, the usual dose of the drug should be administered. In patients with renal dysfunction (creatinine clearance <50 ml/min) the dosage regimen should be adjusted as described in paragraph 2.6 "Posology and method of administration".

2.4.3 Use in pregnancy:
Fluconazole administration in pregnancy should be avoided, except in the case of patients with severe and life threatening fungal infections, in which the drug can be administered if the expected benefits from the treatment outweigh potential risks of toxic effects on the fetus.

2.4.4 Use in breast feeding:
Fluconazole administration in breast feeding mothers is not recommended.

2.4.5 Use in children:
See Posology.

2.4.6 Effects on ability to drive and use machines:
Fluconazole does not impair a patient’s ability to drive or use machinery.

2.4.7 Special warnings for the included excipients:
Stabilanol capsules contain lactose. This may make them unsuitable for people with lactose insufficiency, galactosemia or glucose-galactose malabsorption syndrome. These conditions affect the way people metabolize lactose. Your doctor may have told you if you have these conditions.

2.5 Drug Interactions:
Fluconazole may interact with other drugs such as anticoagulants, sulfonylureas, hydrochlorothiazide, phenytoin, oral contraceptives, rifampicin, cyclosporin, theophylline, terfenadine, zidovudine and astemizole if you receiving any of these drugs, consult your doctor. Co-administration with chlorthiazide is not recommended.

2.6 Possibility of hepatotoxicity:
As absorption of orally administered Fluconazole is rapid and complete, the Fluconazole daily dose is the same for both oral and intravenous administration.

The Fluconazole daily dose should be based on the type and severity of the mycotic infection. Most cases of vaginal candidiasis respond therapeutically to single dose administration.

For infections requiring multiple dose administration, treatment should be continued until the clinical parameters and laboratory examinations show resolution of the active mycotic infection. Insufficient duration of Fluconazole treatment may result in a relapse of the active infection. Patients with AIDS and cryptococcal meningitis or recurrent oropharyngeal candidiasis usually require preventive treatment to reduce the occurrence of relapses.

Adults

1a. For the treatment of cryptococcal meningitis and cryptococcal infections of other body areas, the usual dose is 400mg on the first day of the treatment followed by a dose of 200-400mg once daily. The duration of treatment in
cryptococcal infections depends on the clinical mycological response but usually lasts from 6 to 12 weeks in cryptococcal meningitis and 10 to 12 weeks after a negative result of the CSF culture.

1. For the prevention of cryptococcal meningitis relapse in patients with AIDS, after the completion of the initial treatment it is possible to administer Fluconazole indefinitely at a daily dose of 100-200mg.

2. For the treatment of candidaemia, generalized candidiasis and other severe candidal infections, the usual dose is 400mg on the first day of the treatment, followed by a daily dose of 200mg. Depending on the clinical response of the patient, the dose may be increased to 400mg daily. The treatment's duration depends on the clinical response of the patients.

3. With regard to deep endocarditis, doses of 200-400mg daily for a duration of treatment which may last 2 years may prove to be necessary. Duration of treatment should be adapted in every case.

4. For the treatment of oropharyngeal candidiasis, the usual dose is 50-100mg daily once daily for 7-14 days. If necessary, the treatment may be continued for a longer time span in patients with a severe disorder of the immune system.

5. For the treatment of atrophic oral candidiasis associated with artificial dentures, the usual Fluconazole dose is 50mg once daily for 14 days, concurrently administered with the application of local antiseptic measures to the denture.

6. For the treatment of other candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

7. For the treatment of vaginal candidiasis and candida balanitis, 150mg of Fluconazole should be administered orally as a single dose.

8. For the treatment of skin infections including infections of the feet, of the thin skin layer and of the bikini line, as well as acne vulgaris and infections caused by C. albicans, the recommended dose is 150mg once weekly or 50mg once daily. The duration of treatment usually extends from 2 to 4 weeks but in particular infection of the feet may require treatment for up to 6 weeks. For acne vulgaris, the recommended dose is 50mg once daily for 2 to 4 weeks.

7.1. Onychomycosis, the recommended dose is 150mg once weekly. Treatment is continued until the infected nail is replaced due to normal nail growth. Normally it takes about 3 to 6 months and 6 to 12 months respectively for fingernails and toenails to grow. Of course the growth rate depends on the person, age and the stage of the infection before treatment.

7.2. For the prevention of fungal infections in patients with an increased risk of these infections as a result of neutropenia following cytotoxic (chemotherapeutic) treatment, the recommended dose is 6-12mg/kg daily, depending on the severity of the disease.

8. For the treatment of vaginal candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

9. For the treatment of deep fungal infections in patients with an increased risk of generalized infection e.g. patients who are expected to have severe underlying diseases such as AIDS and cancer. As with other azoles, infections caused by Aspergillus species and Candida species are excluded.

10. For the treatment of deep endocarditis, doses of 200-400mg daily for a duration of treatment which may last 2 years may prove to be necessary. Duration of treatment should be adapted in every case.

11. For the treatment of atrophic oral candidiasis associated with artificial dentures, the usual Fluconazole dose is 50mg once daily for 14 days, concurrently administered with the application of local antiseptic measures to the denture.

12. For the treatment of other candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

13. For the treatment of vaginal candidiasis and candida balanitis, 150mg of Fluconazole should be administered orally as a single dose.

14. For the treatment of skin infections including infections of the feet, of the thin skin layer and of the bikini line, as well as acne vulgaris and infections caused by C. albicans, the recommended dose is 150mg once weekly or 50mg once daily. The duration of treatment usually extends from 2 to 4 weeks but in particular infection of the feet may require treatment for up to 6 weeks. For acne vulgaris, the recommended dose is 50mg once daily for 2 to 4 weeks.

15. For onychomycosis, the recommended dose is 150mg once weekly. Treatment is continued until the infected nail is replaced due to normal nail growth. Normally it takes about 3 to 6 months and 6 to 12 months respectively for fingernails and toenails to grow. Of course the growth rate depends on the person, age and the stage of the infection before treatment.

16. For the treatment of vaginal candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

17. For the treatment of deep fungal infections in patients with an increased risk of generalized infection e.g. patients who are expected to have severe underlying diseases such as AIDS and cancer. As with other azoles, infections caused by Aspergillus species and Candida species are excluded.

18. For the treatment of deep endocarditis, doses of 200-400mg daily for a duration of treatment which may last 2 years may prove to be necessary. Duration of treatment should be adapted in every case.

19. For the treatment of atrophic oral candidiasis associated with artificial dentures, the usual Fluconazole dose is 50mg once daily for 14 days, concurrently administered with the application of local antiseptic measures to the denture.

20. For the treatment of other candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

21. For the treatment of vaginal candidiasis and candida balanitis, 150mg of Fluconazole should be administered orally as a single dose.

22. For the treatment of skin infections including infections of the feet, of the thin skin layer and of the bikini line, as well as acne vulgaris and infections caused by C. albicans, the recommended dose is 150mg once weekly or 50mg once daily. The duration of treatment usually extends from 2 to 4 weeks but in particular infection of the feet may require treatment for up to 6 weeks. For acne vulgaris, the recommended dose is 50mg once daily for 2 to 4 weeks.

23. For onychomycosis, the recommended dose is 150mg once weekly. Treatment is continued until the infected nail is replaced due to normal nail growth. Normally it takes about 3 to 6 months and 6 to 12 months respectively for fingernails and toenails to grow. Of course the growth rate depends on the person, age and the stage of the infection before treatment.

24. For the treatment of vaginal candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

25. For the treatment of deep fungal infections in patients with an increased risk of generalized infection e.g. patients who are expected to have severe underlying diseases such as AIDS and cancer. As with other azoles, infections caused by Aspergillus species and Candida species are excluded.

26. For the treatment of deep endocarditis, doses of 200-400mg daily for a duration of treatment which may last 2 years may prove to be necessary. Duration of treatment should be adapted in every case.

27. For the treatment of atrophic oral candidiasis associated with artificial dentures, the usual Fluconazole dose is 50mg once daily for 14 days, concurrently administered with the application of local antiseptic measures to the denture.

28. For the treatment of other candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

29. For the treatment of vaginal candidiasis and candida balanitis, 150mg of Fluconazole should be administered orally as a single dose.

30. For the treatment of skin infections including infections of the feet, of the thin skin layer and of the bikini line, as well as acne vulgaris and infections caused by C. albicans, the recommended dose is 150mg once weekly or 50mg once daily. The duration of treatment usually extends from 2 to 4 weeks but in particular infection of the feet may require treatment for up to 6 weeks. For acne vulgaris, the recommended dose is 50mg once daily for 2 to 4 weeks.

31. For onychomycosis, the recommended dose is 150mg once weekly. Treatment is continued until the infected nail is replaced due to normal nail growth. Normally it takes about 3 to 6 months and 6 to 12 months respectively for fingernails and toenails to grow. Of course the growth rate depends on the person, age and the stage of the infection before treatment.

32. For the treatment of vaginal candidiasis infections of the mucosa (except vaginal candidiasis, see below), e.g. esophagitis, non-invasive bronchopulmonary infections, candiduria, chronic mucocutaneous candidiasis etc. the usual Fluconazole dose is 50-100mg daily for 14-30 days.

33. For the treatment of deep fungal infections in patients with an increased risk of generalized infection e.g. patients who are expected to have severe underlying diseases such as AIDS and cancer. As with other azoles, infections caused by Aspergillus species and Candida species are excluded.

34. For the treatment of deep endocarditis, doses of 200-400mg daily for a duration of treatment which may last 2 years may prove to be necessary. Duration of treatment should be adapted in every case.

35. For the treatment of atrophic oral candidiasis associated with artificial dentures, the usual Fluconazole dose is 50mg once daily for 14 days, concurrently administered with the application of local antiseptic measures to the denture.
Pharmathen Approval Form

File name: Stabilanol 28-SI1-O02.4.indd
Product: Stabilanol caps 50, 100 & 150mg, sol. 100mg/50ml
Dimensions: 148 x 260 mm
Customer: [ ]
Customer code: [ ]

Please verify that following list has been checked:
- Item code
- Dimensions
- Reg. No.
- Address
- Batch and Expiry
- PL No.
- POM Box
- Barcode
- Phone No.
- Pantone swatches

ARTWORK APPROVAL

Person name: [ ]
Department: [ ]
Sign: [ ]
Date: [ ]

ORDER

Person name: [ ]
Department: [ ]
Sign: [ ]
Date: [ ]